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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,323	05/31/2005	Hiroaki Matsuno	259979US0PCT	7538

22850 7590 06/23/2009

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

NOTIFICATION DATE	DELIVERY MODE
06/23/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/509,323	MATSUNO ET AL.	
	Examiner	Art Unit	
	MINA HAGHIGHATIAN	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 10-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☒ Claim(s) *1-4 and 10-14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Examiner of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Haghighatian.

Receipt is acknowledged of the Amendments and Remarks filed on 07/17/08. Claim 1 has been amended while no claims have been cancelled or newly added. Accordingly claims **1-4 and 10-14** remain pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellini et al. (US Pat. 6,251,876) in view of Collins et al. (US Pat. 6,096,728).

Bellini et al. disclose an autocross-linked **hyaluronic acid** (HA) containing intra- and inter chain ester bonds where autocross-linked HA can be synthesized from HA having a molecular weight in the range from 50 kDa to 5,000 kDa that is used to treat

arthropathies (Column 3, lines 20-38). It is disclosed that the autocross-linked HA can also contain external esters by cross linking with mono or polyvalent alcohol (Column 5, lines 8-23). It is disclosed that the composition can include **an antibiotic** (Column 4, lines 6-9, Claim 4). Bellini discloses suitable antibiotics to include erythromycin, lincomycin, etc (see col. 8, lines 17-22).

Collins et al. disclose the combination of a drug substance and cross-linked hyaluronan gels and that the drug can be used to treat inflammatory conditions of a joint such as gentamicin, vancomycin and structurally related antimicrobials (Column 7, lines 10-19, Column 28, lines 31-38, Column 32, lines 34-50).

The claims are interpreted to include two embodiments (In light of the language of “and/or”). One embodiment requires a composition comprising an antibiotic and a hyaluronic acid. Various infections are considered “intended use” and are not given patentable weight in a product claim. Thus the above cited references meet all the limitations of the said claims. Bellini et al disclose hyaluronic acid in combination with an antibiotic. Collins et al disclose the specific antibiotic of claim 13.

It would have been obvious to one of ordinary skill in the art at the time the invention was made, given the general teachings of the formulations of Bellini et al comprising a hyaluronic acid and active agents such as antibiotics, to have looked in the art for other and specific antibiotics for combination with the formulations of Bellini et al, as taught by Collins et al with reasonable expectation of successfully preparing a formulation that delivers the active agents to the site of action. In other words, the

claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 1-4, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyoshi et al (WO 0027405, as evidenced by its US 6,635,267) in view of Collins et al. (US Pat. 6,096,728).

Miyoshi et al 'US '267 teach a gel made of **hyaluronic acid alone** which is hardly soluble in a neutral aqueous solution and has fluidity enough to be easily ejectable from an injector (see abstract). The molecular weight of the HA to be used in the present invention is preferably within the range of from about $1x10^5$ to about $1x10^7$ Daltons (see col. 6, lines 6-10). The HA gel according to the invention can be solubilized through degradation by treatment under accelerating conditions for acid hydrolysis of HA (see col. 6, lines 29-33). Miyoshi lacks disclosure on combining the HA gel with antibiotics. This deficiency is cured by Collins et al.

Collins et al. disclose the combination of a drug substance and cross-linked hyaluronan gels and that the drug can be used to treat inflammatory conditions of a joint

such as gentamicin, vancomycin and structurally related antimicrobials (Column 7, lines 10-19, Column 28, lines 31-38, Column 32, lines 34-50).

It would have been obvious to one of ordinary skill in the art at the time the invention was made, given the general teachings of the formulations of Miyoshi et al comprising a cross-linked hyaluronic acid gel and active agents, to have looked in the art for other and specific active agents such as antibiotics for combination with the formulations of Myioshi et al, as taught by Collins et al with reasonable expectation of successfully preparing a formulation that delivers the active agents to the site of action. In other words, the claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 1-4, 10-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawata et al (WO 0157093, as evidenced by its US 7,014,860) in view of Collins et al. (US Pat. 6,096,728).

Kawata et al teach production of hyaluronic acid gel which comprises keeping hyaluronic acid in water at a hyaluronic acid concentration of at least 5 wt% in the

presence of an acid component in an amount at least equimolar with the carboxyl groups in the hyaluronic acid (se abstract). It is disclosed that "The present invention provides a hardly water soluble hyaluronic acid gel made of **hyaluronic acid alone** with transparency. The hyaluronic acid gel according to the present invention retains the structure of the biologically inherent hyaluronic acid by virtue of obviation of use of crosslinkers, and is excellently safe and biocompatible. Therefore, it is useful as a biomedical material such as an injection for treatment of arthrosis, an embolizing material, an injection for a soft tissue and an artificial vitreous body" (see col. 6, lines 22-30).

Kawata et al also discloses that the molecular weight of the HA to be used in the present invention is preferably within the range of from about $1x10^5$ to about $1x10^7$ Daltons (see col. 6, lines 62-67). The HA gel according to the invention can be solubilized through degradation by treatment under accelerating conditions for acid hydrolysis of HA (see col. 7, lines 31-36). Kawata et al lacks disclosure on combining the HA gel with antibiotics. This deficiency is cured by Collins et al.

Collins et al. disclose the combination of a drug substance and cross-linked hyaluronan gels and that the drug can be used to treat inflammatory conditions of a joint such as gentamicin, vancomycin and structurally related antimicrobials (Column 7, lines 10-19, Column 28, lines 31-38, Column 32, lines 34-50).

It would have been obvious to one of ordinary skill in the art at the time the invention was made, given the general teachings of the formulations of Kawata et al comprising a cross-linked hyaluronic acid gel and active agents, to have looked in the art for other and specific active agents such as antibiotics for combination with the formulations of Kawata et al, as taught by Collins et al with reasonable expectation of successfully preparing a formulation that delivers the active agents to the site of action. In other words, the claims would have been obvious because the substitution of one known element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to

be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 10-14 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 18-21 of U.S. Patent No. 7,014,860 in view of 6,096,728 (Collins et al). An obviousness-type double patenting rejection is appropriate because while the conflicting claims are not identical, the examined claims are not patentably distinct from the reference claims because the examined claims would have been obvious over the reference claims in view of 6,096,728 (Collins et al).

Here, instant claims are drawn to a composition comprising an antibiotic and a hyaluronic acid and/or a hyaluronic acid gel, wherein the hyaluronic acid gel is crosslinked hyaluronic acid made of hyaluronic acid having a weight average primary molecular weight greater than 800,000 wherein the hgaluronic acid gel is prepared by dissolving hgaluronic acid in an aqueous solution at an acidic pH with no crosslinkers to form the hgaluronic gel and wherein the antibiotic is added to the formed hyaluronic gel.

The reference claims are drawn to a biomedical material which contains a transparent gel consisting of hyaluronic acid or a salt thereof; a second acid or a salt thereof; and water; wherein the transparent gel does not contain any cross-linkers, and wherein the hyaluronic acid gel dissolves in a neutral aqueous solution.

The difference is that the reference claims do not recite or require the addition of an antibiotic to the gel. Collins et al remedies this deficiency. Collins et al teach a

composition comprising hyaluronic acid and active agents such as antibiotics for effective drug delivery to the sites. It would have been obvious to one of ordinary skill in the art to have implemented the teachings of Collins et al on the addition of an antibiotic to the formulations of the reference claims with reasonable expectation of successful delivery of active agents to the desired site of action.

Claims 1-4 and 10-14 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,635,267 in view of 6,096,728 (Collins et al). An obviousness-type double patenting rejection is appropriate because while the conflicting claims are not identical, the examined claims are not patentably distinct from the reference claims because the examined claims would have been obvious over the reference claims in view of 6,096,728 (Collins et al).

Here, instant claims are drawn to a composition comprising an antibiotic and a hyaluronic acid and/or a hyaluronic acid gel, wherein the hyaluronic acid gel is crosslinked hyaluronic acid made of hyaluronic acid having a weight average primary molecular weight greater than 800,000 wherein the hgaluronic acid gel is prepared by dissolving hgaluronic acid in an aqueous solution at an acidic pH with no crosslinkers to form the hgaluronic gel and wherein the antibiotic is added to the formed hyaluronic gel.

The reference claims are drawn to a hyaluronic acid gel comprising water and hyaluronic acid, wherein the said hyaluronic acid is not in the form of a complex with cationic polymer and wherein the gel is auto cross-linked.

The difference is that the reference claims do not recite or require the addition of an antibiotic to the gel. Collins et al remedies this deficiency. Collins et al teach a composition comprising hyaluronic acid and active agents such as antibiotics for effective drug delivery to the sites. It would have been obvious to one of ordinary skill in the art to have implemented the teachings of Collins et al on the addition of an antibiotic to the formulations of the reference claims with reasonable expectation of successful delivery of active agents to the desired site of action.

Claims 1-4 and 10-14 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 24, 26 and 29 of U.S. Patent No. 6,638,538 in view of 6,096,728 (Collins et al). An obviousness-type double patenting rejection is appropriate because while the conflicting claims are not identical, the examined claims are not patentably distinct from the reference claims because the examined claims would have been obvious over the reference claims in view of 6,096,728 (Collins et al).

Here, instant claims are drawn to a composition comprising an antibiotic and a hyaluronic acid and/or a hyaluronic acid gel, wherein the hyaluronic acid gel is crosslinked hyaluronic acid made of hyaluronic acid having a weight average primary molecular weight greater than 800,000 wherein the hgaluronic acid gel is prepared by dissolving hgaluronic acid in an aqueous solution at an acidic pH with no crosslinkers to form the hgaluronic gel and wherein the antibiotic is added to the formed hyaluronic gel.

The reference claims are drawn to a composition comprising hyaluronic acid and a polymer wherein the process does not require presence of any cross-linkers, and wherein the hyaluronic acid gel dissolves in a neutral aqueous solution.

The difference is that the reference claims do not recite or require the addition of an antibiotic to the gel. Collins et al remedies this deficiency. Collins et al teach a composition comprising hyaluronic acid and active agents such as antibiotics for effective drug delivery to the sites. It would have been obvious to one of ordinary skill in the art to have implemented the teachings of Collins et al on the addition of an antibiotic to the formulations of the reference claims with reasonable expectation of successful delivery of active agents to the desired site of action.

Claims 1-4 and 10-14 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,387,413 in view of 6,096,728 (Collins et al). An obviousness-type double patenting rejection is appropriate because while the conflicting claims are not identical, the examined claims are not patentably distinct from the reference claims because the examined claims would have been obvious over the reference claims in view of 6,096,728 (Collins et al).

Here, instant claims are drawn to a composition comprising an antibiotic and a hyaluronic acid and/or a hyaluronic acid gel, wherein the hyaluronic acid gel is crosslinked hyaluronic acid made of hyaluronic acid having a weight average primary molecular weight greater than 800,000 wherein the hgaluronic acid gel is prepared by

dissolving hgaluronic acid in an aqueous solution at an acidic pH with no crosslinkers to form the hgaluronic gel and wherein the antibiotic is added to the formed hyaluronic gel.

The reference claims are drawn to a gel comprising hyaluronic acid and a biomedical material which contains a gel consisting of hyaluronic acid or a salt thereof; wherein the gel does not contain any cross-linkers, and wherein the hyaluronic acid gel dissolves in a neutral aqueous solution.

The difference is that the reference claims do not recite or require the addition of an antibiotic to the gel. Collins et al remedies this deficiency. Collins et al teach a composition comprising hyaluronic acid and active agents such as antibiotics for effective drug delivery to the sites. It would have been obvious to one of ordinary skill in the art to have implemented the teachings of Collins et al on the addition of an antibiotic to the formulations of the reference claims with reasonable expectation of successful delivery of active agents to the desired site of action.

Response to Arguments

Applicant's arguments with respect to claim 07/17/08 have been considered but are moot in view of the new ground(s) of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINA HAGHIGHATIAN whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

Mina Haghighatian
Primary Examiner
Art Unit 1616